Citation:

Flint AJ, Hu FB, Glynn RJ, Jensen MK, Franz M, Sampson L, Rimm EB. Whole grains and incident hypertension in men. *Am J Clin Nutr*. 2009 Sep; 90 (3): 493-498.

PubMed ID: 19571218

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To estimate the association of whole grain intake and risk of incident hypertension (HTN) in a large prospective cohort of men.

Inclusion Criteria:

Participants of the Health Professionals Follow-up Study, a prospective cohort of male health professionals age 40-75 years at enrollment in 1986.

Exclusion Criteria:

Participants with prevalent cancer, stroke, or coronary heart disease (CHD) at baseline; a diagnosis of HTN at baseline or missing diet information.

Description of Study Protocol:

Recruitment

Participants completed a baseline mailed questionnaire at enrollment in 1986.

Design

Prospective cohort study.

Dietary Intake/Dietary Assessment Methodology

A validated semi-quantitative food-frequency questionnaire (FFQ) designed to assess average food intakes over the previous year was used, and included questions on consumption of grain foods. Daily intakes of whole grains, bran and germ were calculated.

Blinding Used

Not applicable.

Intervention

Not applicable.

Statistical Analysis

- Cox proportional hazards regression was used to model the relation between time-varying whole grain intake and incident HTN
- Exploratory analyses used additional terms for whole grain constituents (naturally occurring and added bran and naturally occurring and added germ, potassium, magnesium, total fiber, folate and cereal fiber).

Data Collection Summary:

Timing of Measurements

- Baseline survey: Medical history, dietary intake, lifestyle and demographic information
- Follow-up questionnaires every two years: Interim medical history and updated lifestyle characteristics
- Follow-up questionnaires every four years: FFQ.

Dependent Variables

Incident HTN: Self-reported every two years by asking whether the participant "had any of the following professionally diagnosed illnesses," which included "high blood pressure."

Independent Variables

Whole grain intake: Participants assigned to quintiles of whole grain intake by using the cumulative average update method (average of all past measures).

Control Variables

- Age
- Energy intake
- Family history of HTN
- Family history of CHD
- Smoking
- Marital status
- Alcohol
- Profession
- Height
- Fruit and vegetable intakes
- Sodium intake
- Physical activity
- Multivitamin use
- Cholesterol screening.

Description of Actual Data Sample:

- *Initial N:* 51,529
- *Attrition (final N):* 31,684 (after exclusions)
- *Age:* 40-75 years at baseline
- *Ethnicity:* Not reported
- *Other relevant demographics:* Health professionals
- *Anthropometrics:* None
- *Location:* United States.

Summary of Results:

Key Findings

- Whole grain intake was inversely associated with HTN. In multivariate adjusted analyses, the relative risk of incident HTN in the lowest compared to the highest quintile of whole grain intake was 0.81 (95% CI: 0.75, 0.87; P for trend <0.0001)
- Total bran intake inversely associated with HTN. In multivariate adjusted analyses, the relative risk of incident HTN in the lowest compared to the highest quintile of total bran intake was 0.85 (95% CI: 0.78, 0.92; P for trend=0.002)
- Total germ intake was not significantly associated with HTN in multivariate adjusted analyses. The relative risk of incident HTN in the lowest compared to the highest quintile of total germ intake was 0.96 (95% CI: 0.88, 1.04; P for trend=0.11).

Other Findings

Body mass index was not included in the main multivariate model, because it was presumed to play a role in the causal pathway between whole grain intake and HTN. When BMI was added to the multivariate model, the inverse association was slightly attenuated (risk ratio for highest vs. lowest intake quintile: 0.87; 95% CI: 0.81-0.93).

Author Conclusion:

Whole grains and total bran were inversely associated with new onset HTN.

Reviewer Comments:

Strengths

- *Dietary intake and other covariates were updated throughout the study*
- *Self-report of HTN was previously validated in the study cohort*
- *Analyses were adjusted for many potential confounders, including lifestyle behaviors*
- *Exposure measurement used a food composition database to estimate whole grain intake in grams per day from all foods (rather than summing servings of specific foods, which may be less accurate)*
- *Diet was measured with a validated FFQ.*

Limitations

- *Potential measurement error for self-reported exposures and outcome*
- *Potential unmeasured confounders.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	N/A
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	N/A

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	???
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	N/A
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A

3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	N/A
4.1.	Were follow-up methods described and the same for all groups?	N/A
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	N/A
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	N/A
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	N/A
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	N/A
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes

6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	N/A
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	N/A

8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	???
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	No
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes